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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/708,276	11/07/2000	Gary J. Nabel	1708642/94	1399

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EXAMINER
SANDALS, WILLIAM O

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/708,276	Nabel
Examiner	**Art Unit**
William Sandals	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 27, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *2-34 and 36-42* is/are pending in the application.

4a) Of the above, claim(s) *2-28* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *29-34 and 36-42* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

4) ☐ Interview Summary (PTO-413) Paper No(s). _____

DETAILED ACTION

Response to Amendment

1. The declaration filed in Paper No. 11 on August 27, 2002 under 37 CFR 1.131 is sufficient to overcome the US 6,110,744 reference.

Response to Arguments

2. Arguments in Paper No. 11 have overcome the objection to the specification, New Matter, in the previous office action, and the objection is withdrawn.

3. Arguments and the declaration under 37 CFR 1.131 in Paper No. 11 have overcome the rejection of claims 29 and 32-35 under 35 USC 102e in the previous office action, and the rejection is withdrawn.

4. Arguments and the declaration under 37 CFR 1.131 in Paper No. 11 have overcome the rejection of claims 29-41 under 35 USC 103 in the previous office action, and the rejection is withdrawn.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 29 and 32-34 are rejected under 35 U.S.C. 102(e) as being anticipated by US 5,672,508 (Gyuris et al.).

Gyuris et al. taught (see especially columns 4, 7, 8, 15 and 19-21) a composition comprising a nucleic acid encoding p27 gene and a catheter. The nucleic acid is contained in a viral particle expression vector, and the composition may also comprise a liposome. The limitation of a "kit" in the preamble of claim 29 connotes nothing more than a collection of items, and US 5,672,508 taught the instant claimed collection of a nucleic acid encoding p27 gene and a catheter for the practice of the invention as taught by Gyuris et al.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,672,508 (Gyuris et al.) each in view of US 5,328,470 (Nabel et al.).

The claims are drawn to a kit (composition) comprising a nucleic acid encoding p27 gene and a catheter, which may be a single balloon catheter or a double balloon catheter. The nucleic acid is contained in a viral particle expression vector, and the composition may also comprise a liposome.

Gyuris et al. taught (see especially columns 4, 7, 8, 15 and 19-21) a composition comprising a nucleic acid encoding p27 gene and a catheter. The nucleic acid is contained in a viral particle expression vector, and the composition may also comprise a liposome. The catheter was taught to be useful to deliver the desired recombinant nucleic acid encoding a p27 protein to the cells of a blood vessel to treat restenosis.

Gyuris et al. did not teach that the catheter was a single balloon or double balloon catheter.

Nabel et al. taught at the abstract and columns 4-5 a single and a double balloon catheter for the direct delivery of recombinant nucleic acids encoding genes to the walls of blood vessels (in treating restenosis).

It would have been obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of Gyuris et al. with the teachings of Nabel et al. to produce the instant invention. Each of Gyuris et al. and Nabel et al. make obvious the combination of a nucleic acid and a catheter for treating vascular diseases, and Nabel et al. also teaches that single and double balloon catheters were useful for delivering recombinant nucleic acids encoding genes for treating restenosis (a vascular disease).

One of ordinary skill in the art would have been motivated to combine the teachings of Gyuris et al. with the teachings of Nabel et al. to produce the instant invention because Gyuris et al. teach that the recombinant nucleic acid encoding a p27 gene is useful and desirable to be delivered to the wall of blood vessels, and Nabel et al. taught the use of a single balloon or double balloon catheter was desirable and useful to deliver recombinant genes to the walls of a blood vessel in order to treat organ specific locations in an animal. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Gyuris et al. and Nabel et al.

9. Claims 29-34 and 36-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gyuris et al. and Nabel et al. as applied to claims 29-34 above, and further in view of US 5,962,424 (Hallahan et al.).

The claims are drawn to the invention as described above, and also where the nucleic acid encoding p27 also encodes a cytotoxic protein (thymidine kinase, cytosine deaminase or nitric

oxide synthetase; TK , CD or NOS), which may be a fusion protein with p27. p27 may be operatively linked to the gene encoding the cytotoxic protein which may be a dicistronic unit.

Gyuris et al. and Nabel et al. taught the invention as described above. Gyuris et al. taught the equivalent use of recombinant nucleic acids encoding p27 and p21.

Gyuris et al. and Nabel et al. did not teach that the nucleic acid encoding p27 may also encode a cytotoxic protein, where the gene may be thymidine kinase, cytosine deaminase or nitric oxide synthetase.

Hallahan et al. taught (see especially columns 2-6 and the claims) a nucleic acid encoding a p21 gene and a balloon catheter where the p21 gene was operatively linked to a cytotoxic thymidine kinase gene or cytosine deaminase gene, which may be fusion protein, where the nucleic acid may be a viral expression vector in a liposome, in a method of treatment of restenosis.

It would have been obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of Gyuris et al. and Nabel et al. with the teachings of Hallahan et al. to produce the instant invention. Each of Gyuris et al., Nabel et al. and Hallahan et al. make obvious the combination of a nucleic acid and a catheter because each of Gyuris et al., Nabel et al. and Hallahan et al. taught the use of a combination of a recombinant nucleic acid and a catheter in a method of treatment of vascular disease (restenosis), where Hallahan et al. teach the usefulness of a recombinant fusion nucleic acid encoding a cytotoxic protein (TK) in the combination.

One of ordinary skill in the art would have been motivated to combine the teachings of Gyuris et al. and Nabel et al. with the teachings of Hallahan et al. to produce the instant invention because Gyuris et a. taught that the gene encoding p21 may be used as an equivalent to the gene encoding p27 in a method of treating restenosis and Hallahan et al. taught that a fusion gene of p21 and a gene encoding a cytotoxic protein (thymidine kinase) results in the useful and desirable reduction of intimal hyperplasia in the blood vessel in a method of treatment of vascular disease (restenosis). Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Gyuris et al. and Nabel et al. and Hallahan et al.

Thymidine kinase, cytosine deaminase or nitric oxide synthetase are listed as equivalents for the practice of the method of treating restenosis at page 8, line 18 bridging to page 9, line 2 in the instant specification. Therefore, it would have been an obvious choice within the purview of one of ordinary skill in the art to use any one of thymidine kinase, cytosine deaminase or nitric oxide synthetase in the method of treating restenosis.

Conclusion

10. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If

applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Zeta Adams, whose telephone number is (703) 305-3291.

William Sandals, Ph.D.

Examiner

November 24, 2002